AMENDMENTS TO THE CLAIMS

1. (Currently Amended) An improved antisense oligonucleotide between 6 and about 50 bases in length, wherein the improvement comprises substitution of ~~comprising at least~~ one or more naturally occurring backbone linkage with a non-naturally occurring backbone linkage and substitution of ~~at least~~ one or more base with a non-naturally occurring base selected from the group consisting of degenerate ~~or universal~~ base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine, wherein said antisense oligonucleotide is able to hybridize~~hybridizes~~ to ~~at least~~ two or more RNA molecules that differ in sequence by ~~at least~~ one or more nucleotide mismatch in the target regions that hybridize to said antisense oligonucleotide, and wherein ~~said~~ one or more non-naturally occurring~~degenerate or universal~~ base ~~of said antisense oligonucleotide~~ is positioned ~~on~~in said antisense oligonucleotide to ~~correspond to said~~align with a nucleotide mismatch position in the target regions of the RNA molecules.

2. (Original) The antisense oligonucleotide of Claim 1, wherein no more than about 50% of said bases are universal and/or degenerate bases.

3. (Currently Amended) An improved antisense oligonucleotide having a RNA targeting region, wherein the improvement comprises ~~comprising a first and a second non-RNase H recruiting region of between 3 and about 15 bases, and~~ a RNase ~~H~~ recruiting region ~~between 3 and about 15 bases~~, wherein ~~at least~~ one or more base of said antisense oligonucleotide is a non-naturally occurring base selected from the group consisting of a ~~of said bases are universal and/or~~ degenerate ~~bases~~ base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine, and~~,~~ wherein said antisense oligonucleotide is able to hybridze~~hybridizes~~ to ~~at least~~ two or more RNA molecules that differ in sequence by ~~at least~~ one or more nucleotide mismatch in the target regions that hybridize to said antisense oligonucleotide, and wherein ~~said degenerate or universal~~one or more non-naturally occurring base ~~of said antisense oligonucleotide~~ is positioned ~~on~~in said antisense oligonucleotide to ~~correspond to~~align with a ~~said~~ nucleotide mismatch position in the target regions of the RNA molecules.

4. (Original) The antisense oligonucleotide of Claim 3, wherein no more than about 50% of said bases are universal and/or degenerate bases.

5. (Currently Amended) An improved antisense oligonucleotide ~~comprising~~having an RNA targeting region, wherein the improvement comprises a ~~non-RNase H recruiting region and an~~ RNase H recruiting region, wherein the RNA targeting region of said antisense oligonucleotide comprises ~~at least~~ one or more non-naturally occurring base selected from the group consisting of ~~universal and/or~~ degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine, and~~,~~ wherein said antisense oligonucleotide is able to hybridize~~hybridizes~~ to ~~at least~~ two or more RNA molecules that differ in sequence by ~~at least~~ one or more nucleotide mismatch in the target regions that hybridize to said antisense oligonucleotide, and wherein ~~said degenerate or universal~~one or more non-naturally occurring base ~~of said antisense oligonucleotide~~ is positioned ~~on~~in said antisense oligonucleotide to ~~correspond to~~align with a ~~said~~ nucleotide mismatch position in the target regions of the RNA molecules.

6. (Previously Presented) The antisense oligonucleotide of Claim 5, wherein the RNA targeting region comprises no more than about 50% universal and/or degenerate bases.

7. (Currently Amended) An antisense oligonucleotide comprising an RNA targeting region and a RNase L-recruiting region comprising a 2'-5' adenosine oligomer, wherein the RNA targeting region of said antisense oligonucleotide comprises ~~at least~~ one or more non-naturally occurring base selected from the group consisting of ~~universal and/or~~ degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine, and~~,~~ wherein said antisense oligonucleotide is able to hybridize ~~hybridizes~~ to ~~at least~~ two or more RNA molecules that differ in sequence by ~~at least~~ one or more nucleotide mismatch in the target regions that hybridize to said antisense oligonucleotide, and wherein ~~said degenerate or universal~~one or more non-naturally occurring base ~~of said antisense oligonucleotide~~ is positioned ~~on~~in said antisense oligonucleotide to ~~correspond to~~align with a ~~said~~ nucleotide mismatch position in the target regions of the RNA molecules.

8. (Original) The antisense oligonucleotide of Claim 7, wherein said RNA targeting region comprises no more than about 50% universal and/or degenerate bases.

9. (Currently Amended) An antisense oligonucleotide comprising an RNA targeting region and a RNase P recruiting region, wherein the RNA targeting region of said antisense oligonucleotide comprises ~~at least~~ one or more non-naturally occurring base selected from the group consisting of ~~universal and/or~~ degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine, and~~,~~ wherein said antisense oligonucleotide is able to hybridize ~~hybridizes~~ to ~~at least~~ two or more RNA molecules that differ in sequence by ~~at least~~ one or more nucleotide mismatch in the target regions that hybridize to said antisense oligonucleotide, and wherein ~~said degenerate or universal~~one or more non-naturally occurring base ~~of said antisense oligonucleotide~~ is positioned ~~on~~in said antisense oligonucleotide to ~~correspond to~~align with a ~~said~~ nucleotide mismatch position in the target regions of the RNA molecules.

10. (Original) The antisense oligonucleotide of Claim 9, wherein said RNA targeting region comprises no more than about 50% universal and/or degenerate bases.

11. (Currently Amended) A ribozyme comprising an RNA targeting region, which comprises ~~at least~~ one or more non-naturally occurring base selected from the group consisting of ~~universal and/or~~ degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine, wherein said ribozyme is able to hybridize~~hybridizes~~ to ~~at least~~ two or more RNA molecules that differ in sequence by ~~at least~~ one or more nucleotide mismatch in the target regions that hybridize to said ribozyme, and wherein ~~said degenerate or universal~~one or more non-naturally occurring base ~~of said ribozyme~~ is positioned ~~on~~in said ~~antisense oligonucleotide~~ribozyme to ~~correspond to~~align with a ~~said~~ nucleotide mismatch position in the target regions of the RNA molecules.

12. (Original) The ribozyme of Claim 11, wherein said RNA targeting region comprises no more than about 50% universal and/or degenerate bases.

13. -19. (Canceled)

20. (Currently Amended) The antisense oligonucleotide of claim 1 wherein said antisense oligonucleotide comprises one or more sequence ~~motifs~~ motif with one or more degenerate and/or universal base.

21. (Previously Presented) The antisense oligonucleotide of claim 20 wherein said sequence motif is a CG dinucleotide.

22. (Previously Presented) The antisense oligonucleotide of claim 20 wherein said sequence motif is a poly –G sequence.

23. (New) The antisense oligonucleotide of claim 1 further comprising a universal base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

24. (New) The antisense oligonucleotide of claim 3 further comprising any universal base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

25. (New) The antisense oligonucleotide of claim 5 further comprising a universal base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

26. (New) The antisense oligonucleotide of claim 7 further comprising a universal base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

27. (New) The antisense oligonucleotide of claim 9 further comprising a universal base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

28. (New) The ribozyme of claim 11 further comprising a universal base positioned on said ribozyme to align with a nucleotide mismatch of the RNA target region.

29. (New) The antisense oligonucleotide of claim 1 further comprising an inosine base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

30. (New) The antisense oligonucleotide of claim 3 further comprising an inosine base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

31. (New) The antisense oligonucleotide of claim 5 further comprising an inosine base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

32. (New) The antisense oligonucleotide of claim 7 further comprising an inosine base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

33. (New) The antisense oligonucleotide of claim 9 further comprising an inosine base positioned on said antisense oligonucleotide to align with a nucleotide mismatch of the RNA target region.

34. (New) The ribozyme of claim 11 further comprising an inosine base positioned on said ribozyme to align with a nucleotide mismatch of the RNA target region.

35. (New) In an oligonucleotide with antisense activity, wherein the improvement comprises substitution of one or more naturally occurring backbone linkage with a non-naturally occurring backbone linkage and substitution of one or more base with a non-naturally occurring base selected from the group consisting of degenerate base, 5-nitroindole, 3-nitropyrrole, 4-nitrobenzimidazole, and nebularine.

36. (New) The antisense oligonucleotide of claim 35, wherein said antisense oligonucleotide is able to hybridize to two or more mRNA molecules that differ in sequence by one or more nucleotide mismatch in the target regions that hybridize to said antisense oligonucleotide, and wherein one or more non-naturally occurring base is positioned in said antisense oligonucleotide to align with a nucleotide mismatch position in the target regions of the RNA molecules.